ABSTRACT

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Title of diploma thesis: Optimization of chromatographic parameters for chiral separation of biologically active compounds.

The diploma thesis was focused on the development of a HPLC-UV method for the determination of K 1277 enantiomers of systematic name *N*-(2-((6-chloro-1,2,3,4-tetra-hydroacridin-9-yl)amino)hexyl-2-amino-3-(1H-indole-3-yl) propylamide dihydrochloride, which is one of the compounds from the tacrine-tryptophan hybrids group. These tacrine-tryptophan hybrids could be considered as promising candidates of potential drugs against Alzheimer's disease.

The thesis brings an explanation of basic characteristic of chiral molecules, principles of chiral separation, pathophysiology, clinical manifestation and treatment of Alzheimer's disease and short characteristic of tacrine-tryptophan hybrids in the theoretical section. The aim of my diploma thesis was to find the optimal chromatographic conditions for separation of K 1277 enantiomers synthesized from tacrine and tryptophan fragments.

The experimental part deals with the development of the chiral separation method of K 1277 using HPLC. Based on previous experience, two chiral stationary phases (CSPs) – macrocyclic antibiotic teicoplanin and *tris*(3,5-dimethylfenyl)carbamate cellulose were studied. The successful separation of the enantiomers of K 1277 was achieved in a reverse mode on a stationary phase containing modified cellulose.

The optimization of the separation conditions using the Dionex UltiMate 3000 chromatograph was performed. In the optimized method the following parameters - precision of quantification and stability of the separation during repetition of analyses were evaluated and the value of the limit of detection of the method was determined. In the optimized method, the possibility of analyzing the enantiomers of K1277 after application to human plasma was also evaluated.